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Vincent Cool

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EXAMINER

NIEBAUER, RONALD T

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/562,998	<b>Applicant(s)</b> COOL ET AL.	
	<b>Examiner</b> RONALD T. NIEBAUER	<b>Art Unit</b> 1654	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 September 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/27/05</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of the following species:

Salt: benzyltrimethylammonium chloride

Protecting group: Fmoc

in the reply filed on 9/30/08 is acknowledged. The traversal is on the ground(s) that the IPRP stated that there is unity of invention and that there is not a valid basis for the lack of unity.

The arguments have been considered but are not found persuasive.

Although the applicants refer to the IPRP, the IPRP did not cite documents such as those cited in the instant rejections below. The instant claims do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: PCT Rule 13.2 defines “special technical features” as “those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.” As discussed below, art anticipates the instant claims. Thus the technical features are not a contribution over the prior art and the claims lack unity. Further, there is an examination and search burden for the species due to their mutually exclusive characteristics. Each of the species are structurally distinct and one of skill in the art would not recognize that every alternative would behave in the same way. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species.

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The requirement is still deemed proper and is therefore made FINAL.

In the instant case, each of the elected species was found in the prior art or found to be obvious based on the prior art. Any art that was uncovered in the course of searching for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP, the Markush-type claims have been examined with respect to the elected species and to the extent necessary to determine patentability.

Since applicant elected Fmoc, claims 14-15 do not read on the elected species. Since the art cited below reads on claim 14, claim 14 is included in the instant rejection.

Claim 15 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/30/08.

Claims 17-18 have been cancelled.

Claims 1-14,16 are under consideration.

#### ***Claim Objections***

Claims 2-3,5-8,16 objected to because of the following informalities:

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Claims 2-3,5-8 refer to  $(X^{n+})_m(Y^{m-})_n$ . However, these variables are only discussed in claim 1. For completeness the meaning of each of the variables should be set forth in each independent claim.

Claim 16b states 'according claim 3'. It appears that the word 'to' should appear after the word 'according'.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Deleted: 11

**Claims 1, ~~12, 16~~** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 refers to 'bio-oligomers'. The specification (page 1 lines 12-16) refers to the term oligomer and gives examples. However, exemplification is not a definition. In the instant case, it is unclear what differentiates a 'bio'-oligomer from an oligomer. The metes and bounds of bio-oligomer has not been clearly set forth and there is not a standard art recognized definition of bio-oligomer. As such, there can be more than one reasonable interpretation of bio-oligomer.

Claim 12 refers to step (d). However, there is no step (d) in claim 2.

Claim 16b states 'with the following amino acid or peptide foreseen in the sequence'. The claim language is awkward and confusing. It is unclear if the language is attempting to limit the claim to certain sequences and if so, it is unclear what a foreseen sequence might be.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**Claims 1,9-11** are rejected under 35 U.S.C. 102(b) as being anticipated by Klingler et al (US 6,472,562).

In example 5 (column 34 lines 1-36) Klingler teach the solid phase synthesis of compounds. Klingler teach the washing of a resin using benzyltrimethylammonium hydroxide (column 34 lines 23-24). As such Klingler meet the active step of claim 1 of the instant invention (i.e. washing) where the salt of Klingler (i.e. benzyltrimethylammonium hydroxide which is a quaternary ammonium salt where Y is hydroxide) meets the limitations as recited in claims 1,9-11 of the instant invention.

Although unclear (see 112 2<sup>nd</sup>) the term 'bio-oligomer' has been given the broadest reasonable interpretation. The compounds of Klingler are interpreted as bio-oligomers.

**Deleted:** Although unclear (see 112 2nd) claim 11 has been interpreted such that the recited elements are alternate elements.

**Claims 1-4,6-10,12-14,16** are rejected under 35 U.S.C. 102(b) as being anticipated by Thaler et al (Helvetica Chimica Acta v74 1991 pages 628-643).

Thaler teach the addition of inorganic salts such as LiCl during solid phase coupling reactions (abstract). Thaler specifically teach that peptides are synthesized such as alanine oligomers Ala<sub>12</sub>-Phe (abstract) (i.e. bio-oligomers). Thaler teach that the salts are specifically used during washing steps (see page 640 section 2 for example). Since Thaler teach the use of LiCl the salt limitations of claims 1,9-10 are met.

Thaler teach deprotecting (i.e. cleaving), washing, and coupling of protected groups (see page 620 section 2, for example Boc-Ala) thus meeting the active steps of claim 2-3 of the instant invention. It is noted that Thaler teach solvents such as DMF (see solution B of step 2 page 640) thus the solvent is neither a chloroform/phenol nor a chloroform/trifluoroethanol mixture. Thaler teach the use of protected amino acids such as Boc-Ala (page 620 section 2) as recited in claim 3 of the instant invention. Thaler teach multiple wash steps (page 620 section 2) thus meeting the limitations of claim 4 of the instant invention. Thaler teach that the washing is carried out with solutions A-S which include the solvent with salt (for example, B is DMF/LiCl see page 640 section 2) thus meeting the active step of claim 6 of the instant invention. Thaler teach the coupling steps in solutions A-C (page 620 section 2) thus meeting the limitations of claim 7 of the instant invention. Thaler teach a washing in solutions A-S after the coupling thus meeting the limitations of claim 8 of the instant invention. Since Thaler teach that solution B, for example, is used for the initial washing and coupling (page 620 section 2) the limitations of claim 12 are met. Thaler teach the use of Fmoc and Boc protecting groups (page 620 section 2) thus meeting the limitations of claims 13-14 of the instant invention. Thaler teach attaching

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amino acids to a resin (page 640 section 1.4 and 2) thus meeting step 16a of the instant invention. Thaler teach the solid phase synthesis process (thus meeting steps b-c of claim 16) followed by cleavage and HPLC analysis (see page 640-642) thus meeting the limitations of claim 16 of the instant invention.

It is noted that the claims state that the washing is 'thorough'. 'Thorough' is defined (page 2 of specification) as effective to remove reagents from the previous step. Since Thaler teach effective synthesis of peptides the washings are necessarily thorough to allow for effective synthesis.

Although unclear (see 112 2<sup>nd</sup>) the term 'bio-oligomer' has been given the broadest reasonable interpretation.

Although unclear (see 112 2<sup>nd</sup>) claim 16b has been interpreted broadly such that any amino acid or peptide sequence can be used.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**Claims 1-10,12-14,16** rejected under 35 U.S.C. 103(a) as being unpatentable over Thaler et al (Helvetica Chimica Acta v74 1991 pages 628-643).

As discussed above, Thaler teach claims 1-4,6-10,12-14,16 of the instant invention.



Thaler does not expressly teach the addition of salt during the cleaving step as recited in claim 5.

Thaler teach that a problem in solid phase synthesis is insufficient solvation which can lead to aggregation (page 628). Thaler also recognize that peptide-resin swelling is an important factor in solid phase synthesis (page 628-629). Thaler teach that salt additives can increase resin swelling and improve coupling yields (Figure 4). Thaler acknowledge that salt additives should be adjusted for the best results (conclusions page 639). Thaler specifically teach the use of salts for the washing and coupling steps (page 640 section 2).

From the teachings of Thaler one would recognize that the goal is to use salt additives to help solvation and to aid in preventing protein aggregation. One would recognize that insufficient solvation and aggregation are possible at all steps of the solid phase synthetic process. As such, one would be motivated to include salts in the solutions that are used in all steps of the solid phase synthesis including the deprotection steps. Thus one would be motivated to use the LiCl, for example (see page 640) in the DMF/piperidin solution that is used during the deprotection steps of Thaler. It is noted that Thaler teach that amide bonds are formed between the amino acid monomers (see abstract for example) as recited in claim 5c. Taken together with the other steps taught by Thaler, the limitations of claim 5 are met.

Since Thaler teach that salt additives can increase resin swelling and improve coupling yields (Figure 4) one would have a reasonable expectation of success. The claims would have been obvious because the technique for improving solid phase synthesis by including salts at specific steps (for example, during deprotection) was part of the ordinary capabilities of a person

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of ordinary skill in the art, in view of teaching of the technique for improving solid phase synthesis at other steps (for example, during coupling and washing). Further, one would be motivated to optimize the process as taught by Thaler (conclusions page 639).

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference.

Although unclear (see 112 2<sup>nd</sup>) the term 'bio-oligomer' has been given the broadest reasonable interpretation.

Although unclear (see 112 2<sup>nd</sup>) claim 16b has been interpreted broadly such that any amino acid or peptide sequence can be used.

**Claims 1,9-11** rejected under 35 U.S.C. 103(a) as being unpatentable over Klingler et al (US 6,472,562).

As discussed above, Klingler teach claims 1,9-11 of the instant invention.

Klingler does not expressly reach the elected species of salt - benzyltrimethylammonium chloride.

In example 5 (column 34 lines 1-36) Klingler teach the solid phase synthesis of compounds. Klingler teach the washing of a resin using benzyltrimethylammonium hydroxide

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(column 34 lines 23-24). One of skill in the art would recognize that the particular salt used in any given process is often optimized. For example Klingler disclose a wide range of salts (column 11 line 64 to column 12 line 20). In addition to the benzyltrimethylammonium hydroxide, one would recognize that numerous other salts would be suitable for the process. In particular benzyltrimethylammonium chloride is structurally and functionally similar to benzyltrimethylammonium hydroxide and one would have a reasonable expectation of success in using benzyltrimethylammonium chloride. In other words, benzyltrimethylammonium chloride and benzyltrimethylammonium hydroxide can be used interchangeably.

In the instant case, the claims would have been obvious because the substitution of one known element (benzyltrimethylammonium chloride) for another (benzyltrimethylammonium hydroxide) would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference.

Although unclear (see 112 2<sup>nd</sup>) the term 'bio-oligomer' has been given the broadest reasonable interpretation. The compounds of Klingler are interpreted as bio-oligomers.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/  
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/  
Examiner, Art Unit 1654

